778 Russian Chemical Bulletin, International Edition, Vol. 52, No. 3, p. 778, March, 2003

4,5-Dihydroisoxazoles from arylcyclopropanes by reactions with nitrosyl chloride activated with sulfur trioxide

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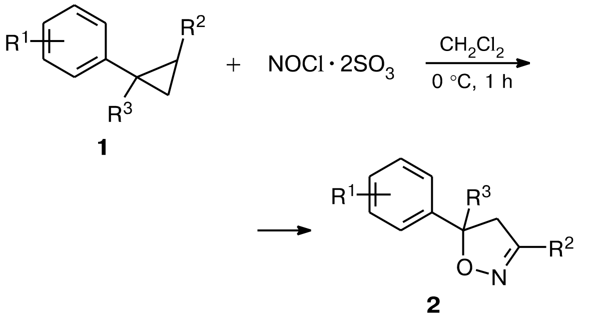
Modern organic synthesis needs convenient starting reagents such as, *e.g.*, an dihydroisoxazole ring.[1] On the one hand, this ring is fairly resistant to various modifications in side chains, while on the other hand, desirable functions can be imparted by transforming the central structure at the final step of the synthesis. For this reason, a search for new reactions and reagents suitable for construction of this heterocycle itself still remains topical.

In the present work, we propose to synthesize 5-aryl-4,5-dihydroisoxazoles by reactions of arylcyclopropanes **1** with $NOCl \cdot 2SO_3$. Unlike previous nitrosating systems,[2—4] this complex makes it possible to obtain isoxazolines under mild conditions (CH_2Cl_2, 0 °C) in high yields from arylcyclopropanes containing both donor and acceptor substituents in the aromatic ring.



	R^1	R^2	R^3	Yield (%)
a	H	H	H	95
b	H	Ph	H	99
c	F	$4\text{-}FC_6H_4$	H	99
d	MeO	$4\text{-}MeOC_6H_4$	H	95
e	H	Me	H	99
f	H	H	Me	93
g	Br	H	H	99
h	I	H	H	99
i	4-MeCO	H	H	62
j	$o\text{-}NO_2/p\text{-}NO_2$ (4 : 1)	H	H	85

Synthesis of 4,5-dihydroisoxazoles 2 from arylcyclopropanes 1 and $NOCl \cdot 2SO_3$ (general procedure). An arylcyclopropane (0.001 mol) in 2 mL of methylene chloride was added at 0 °C to a suspension of $NOCl \cdot 2SO_3$[5] (0.001 mol) in 10 mL of the same solvent. The precipitate dissolved immediately to give a colored solution. After 1 h (TLC), the reaction mixture was neutralized with aqueous sodium carbonate and washed with water. The products were extracted from the aqueous fractions with methylene chloride (3×10 mL); the organic extracts were combined and dried with sodium sulfate. Then the solvent was removed to give a pure crystalline product (the yields are given under the scheme). The NMR spectra and melting points of compounds **2a—h,j** were identical with the literature data.[3,6,7]

5-(4-Acetylphenyl)-4,5-dihydroisoxazole (2i) was obtained from 4-(acetylphenyl)cyclopropane **1i** (0.04 g, 0.25 mmol) and $NOCl \cdot 2SO_3$ (0.06 g, 0.25 mmol) in 15 mL of CH_2Cl_2. Chromatography on SiO_2 in light petroleum—ethyl acetate (3 : 1) gave the title compound (0.3 g, 62%) as colorless crystals, m.p. 55 °C, R_f 0.24. Found (%): C, 69.73; H, 5.46. $C_{11}H_{11}NO_2$. Calculated (%): C, 69.84; H, 5.29. IR (ν/cm^{-1}): 1685 (C=O), 1580, 1280, 820. ^{1}H NMR ($CDCl_3$), δ: 2.58 (s, 3 H, MeCO); 2.87 (ddd, 1 H, CH_2, ^2J = 17.5 Hz, ^3J = 7.6 Hz, ^3J = 1.8 Hz); 3.44 (ddd, 1 H, CH_2, ^2J = 17.5 Hz, ^3J = 11.2 Hz, ^3J = 1.8 Hz); 5.57 (dd, 1 H, CHO, ^3J = 11.2 Hz, ^3J = 7.6 Hz); 7.21 (t, 1 H, CH=, ^3J = 1.8 Hz); 7.40 (d, 2 H, C_6H_4, ^3J = 8.3 Hz); 7.94 (d, 2 H, C_6H_4, ^3J = 8.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 26.63, 43.81, 79.15 (CHO); 125.77, 128.80, 136.85, 145.31, 146.14 (C=N); 197.52 (C=O).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 02-03-33347) and the Ministry of Education of the Russian Federation (the Program "Russian Universities", Project No. 990 879).

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Received October 7, 2002;
in revised form December 11, 2002

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 741—742, March, 2003.